

CHEMICAL THERMODYNAMICS
AND THERMOCHEMISTRY

Thermochemistry of Sesquiterpene Lactone 3,4β-Epoxyarglabin

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Abstract—The enthalpies of dissolution of 3,4β-epoxyarglabin C₁₅H₁₈O₄ are measured via isothermal calorimetry at lactone : 96% ethanol molar ratios of 1 : 6000, 1 : 12000, 1 : 24000 at 298.15 K. The standard enthalpy of dissolution of C₁₅H₁₈O₄ in 96% ethanol is calculated from the obtained data; the value is 40.1 ± 0.4 kJ/mol. The enthalpies of combustion, melting, and formation of 3,4β-epoxyarglabin C₁₅H₁₈O₄ are estimated by approximate means.

Keywords: 3,4β-epoxyarglabin C₁₅H₁₈O₄, standard enthalpies of dissolution, combustion, melting, formation

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INTRODUCTION

The trend toward using terpenoid-derived drugs is constantly growing. Data on their thermochemical and thermodynamic characteristics are required for their standardization and certification in pharmaceutical industry. It should be noted that there are often no such data, especially for structurally complex substances of plant origin.

Data on thermal effects are fundamental in the theory and practice of modeling technological processes. Calorimetry is the main experimental means used in thermochemistry for measuring thermal effects [1].

EXPERIMENTAL

The investigated sesquiterpene lactone 3,4β-epoxyarglabin (**1**) is a derivative of the unique antitumor drug “Arglabin,” developed at AO International Research and Production Holding Phytochemistry (Karaganda, Kazakhstan). This substance of compendial purity was obtained in the laboratory of terpenoid chemistry of AO IRPH Phytochemistry. The sesquiterpene lactone arglabin C₁₅H₁₈O₃ was dissolved in methylene chloride at room temperature; soda (NaHCO₃) was added, then chloroform solution of peracetic acid was added in small portions while stirring. The reaction’s progress was monitored via TLC analysis (thin layer chromatography) [2]. The reaction mixture was transferred to a separatory funnel, treated three times with a 20% aqueous solution of soda, and the organic layer was separated from the aqueous layer. Subsequently, the organic layer was treated three times

with a saturated solution of sodium chloride. The organic layer was dried over magnesium sulfate, and the solvent was evaporated on a rotary evaporator. Further separation via column chromatography on silica gel with petroleum ether : ether (1 : 1) eluent resulted in colorless crystals of C₁₅H₁₈O₄ (3,4β-epoxyarglabin) in 65% yield.

The melting point of C₁₅H₁₈O₄ was then determined. The dried test substance was ground in a mortar into a powder. A capillary tube with a diameter of about 1.5–1.8 mm and a length of 90 mm was then filled with the substance, and the open end of the capillary was immersed in the test substance. To compact the substance, the capillary was passed several times through a glass tube with a diameter of 6–8 mm and a length of 20–30 cm placed vertically on glass. The height of the substance in the capillary after compaction was about 3 mm. The melting point and range were displayed on the front panel and automatically stored in memory. The melting point was determined by averaging three parallel experiments. Automatically determined melting points and ranges corresponded exactly to our visual results. The average melting point of the compound C₁₅H₁₈O₄ was 423 ± 1 K. The instrument was tested and calibrated using certified standards (vanillin (m.p. = 356 K), phenacetin (m.p. = 409 K)) according to the MPA100 OptiMelt manual.

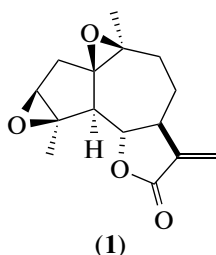
IR spectrum (KBr, ν, cm⁻¹) **1**: 3032, 3001, 2971, 2933, 2887, 1782 (C=O γ-lactone), 1669, 1449, 1439, 1386, 1367, 1343, 1278, 1252, 1179, 1152, 1137, 1129,

1084, 1063, 1052, 1039, 1013, 980, 969, 882, 863, 838, 815, 791, 719, 697, 659, 650, 589, 537, 497, 479.

Mass spectrum of **1** showed a peak of a molecular ion with m/z 262.1 $[M]^+$. Calculated: m/z 262.1200. Found: m/z 262.1197.

According to the literature, 1 β (10 β),3 β (4 β)-diepoxy-5 α ,7 α ,6 β (H)-guai-11(13)-en-12,6-olide (**1**) was obtained later as a result of a multistep synthesis [3].

The geometry of molecule **1** was determined via X-ray diffraction. The structural formula $C_{15}H_{18}O_4$ ($M = 262.307777$) is shown below:



The atomic masses of the elements were taken from [4].

The structure of substance (1) was established as 1 β (10 β),3 β (4 β)-diepoxy-5 α ,7 α ,6 β (H)-guai-11(13)-en-12,6-olide according to the spectral data (IR, ¹H and ¹³C NMR, mass) and the results from X-ray diffraction.

RESULTS AND DISCUSSION

The enthalpies of dissolution of $C_{15}H_{18}O_4$ in 96% ethanol were measured on a DAC-I-IA (differential automatic calorimeter) instrument via isothermal calorimetry ($T = 298.15$ K) at substance : solvent molar ratios of 1 : 6000, 1 : 12000, 1 : 24000 similar to [5]. The main technical data of the calorimeter were: an operating temperature range of 298.15–473 K, an ampoule volume of 8 cm³, a warm-up period of 5 h, a sensitivity in the direct measurement of thermal emf not less than 0.12 μ V/ μ W, a sensitivity in the automatic compensation mode of thermal emf not less than 0.012 μ V/ μ W, and a heat release energy measuring error of no more than 2.0%. Thermal effects were registered using a KSP-4 recording potentiometer and an IP-4 precision integrator in parallel. The pre-thermostating time was 2 h.

Before each experiment, the DAC-I-IA instrument was calibrated by measuring the heat of dissolution of thrice recrystallized potassium chloride at salt : water molar ratios of 1 : 1600, 1 : 2400, 1 : 3200. The average heat of dissolution of KCl in water (at 298.15 K) was 17860 ± 283 J/mol, corresponding to its recommended and reference values [6, 7]. Five parallel experiments were performed for each molar ratio, and the results were averaged. The error in the experiments and the homogeneity of their variances were calculated using mathematical statistics with the Student

and Cochrane criteria [8]. The level of significance of these criteria was 5%. Quantities of $C_{15}H_{18}O_4$ for the calorimetric studies were weighed on Pioneer analytical balance (Ohaus Corporation, United States). The weighing error of one digit in the last place was considered in determining the errors in the enthalpy of dissolution. Our calorimetric studies were conducted with very small quantities because of the difficulty in obtaining $C_{15}H_{18}O_4$.

Analysis of pure 96% ethanol showed that the volume percent of ethyl alcohol was no less than 96.3%, the concentration of fusel oil was 1.66 mg/dm³, the volume fraction of methyl alcohol in terms of anhydrous alcohol was 0.00044. No acetic aldehyde, esters (methyl acetate, ethyl acetate), free acids (other than CO₂), or dry residue of nitrogenous volatile bases and furfural were detected.

The results from our calorimetric determination of the enthalpy of dissolution of 3,4 β -epoxyarglabin $C_{15}H_{18}O_4$ in 96% ethanol at different mole ratios are shown in Table 1.

The averaged values of the experimentally determined enthalpies of dissolution of the compounds ($\Delta H_{\text{diss(I)}}^m$, $\Delta H_{\text{diss(II)}}^m$, $\Delta H_{\text{diss(III)}}^m$) at three mole ratios were subsequently used to calculate ΔH° of the dissolution of $C_{15}H_{18}O_4$ in an infinitely dilute ethanol solution. An equation showing the linear dependence of the enthalpy of dissolution of 3,4 β -epoxyarglabin from its molar concentration (\sqrt{m}) in 96% ethanol was derived using an extrapolation technique similar to the one in [9]:

$$\Delta H_{\text{diss}}^m = 40.1 - 248.9\sqrt{m}. \quad (1)$$

Using Eq. (1), the standard enthalpy of dissolution of 3,4 β -epoxyarglabin in an infinitely dilute 96% ethanol solution was found to be equal to 40.1 ± 0.4 kJ/mol.

The standard enthalpy of combustion $\Delta H_{\text{comb}}^0(298.15)$ of $C_{15}H_{18}O_4$ was calculated using the Karash equation [10] (kcal/mol):

$$\Delta_{\text{comb}}H^0(298.15) = -26.050(4C + H - p) + \sum k_i \Delta_i, \quad (2)$$

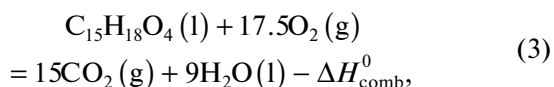
where -26.050 kcal/mol is the heat of C–C, C–H bond rupture and the subsequent formation of CO₂ and H₂O; C is the number of carbon atoms in the compound; H is the number of hydrogen atoms in the compound; p is the number of partially moved electrons in a molecule of the compound; k_i is the number of identical substituents; and Δ_i is the corresponding heat adjustment for the substituent. Equation (2) was used by assuming (a) the valence electrons move from the atoms of the organic compound to the oxygen atoms during combustion; (b) each carbon atom provides four electrons, and each hydrogen atom provides one electron; (c) if the hydrogen in the compound is replaced with another atom or group of atoms, the

Table 1. Enthalpies of dissolution of 3,4 β -epoxyarglabin C₁₅H₁₈O₄ in 96% ethanol at substance : solvent molar ratios of 1 : 6000, 1 : 12000, 1 : 24000

Entry	<i>m</i> , g	ΔH_{diss} , J	ΔH_{diss}^m , kJ/mol
1 : 6000			
1	0.0037	0.3623	25.68
2	0.0037	0.3505	24.85
3	0.0037	0.3586	25.42
4	0.0037	0.3568	25.29
5	0.0037	0.3587	25.43
Average value		$\Delta H_{\text{diss(I)}}^m = 25.33 \pm 0.38$	
1 : 12000			
1	0.0019	0.2132	29.43
2	0.0019	0.2085	28.78
3	0.0019	0.2073	28.62
4	0.0019	0.2121	29.28
5	0.0019	0.2120	29.27
Average value		$\Delta H_{\text{diss(II)}}^m = 29.08 \pm 0.44$	
1 : 24000			
1	0.0009	0.1120	32.64
2	0.0009	0.1142	33.28
3	0.0009	0.1107	32.26
4	0.0009	0.1142	33.28
5	0.0009	0.1138	33.17
Average value		$\Delta H_{\text{diss(III)}}^m = 32.93 \pm 0.57$	

electronic structure of the molecule changes, and the heat of combustion of the compound rises or falls by the amount of the structural adjustment Δ_i ; and the number of electrons moved to oxygen falls by p , the same number of electrons strongly bound to atoms replacing the hydrogen atoms in the compound. The calculated value of $\Delta H_{\text{comb}}^0(298.15)$ for C₁₅H₁₈O₄ was -8337 ± 10 kJ/mol.

According to the reaction of



the standard enthalpy of liquid C₁₅H₁₈O₄ formation was calculated (-137.7 ± 10.1 kJ/mol). The required data for calculating the standard enthalpy of formation of C₁₅H₁₈O₄ $\Delta_f H^0(\text{CO}_2(\text{g}), 298.15) = -393.51 \pm 0.05$ kJ/mol and $\Delta_f H^0(\text{H}_2\text{O}(1), 298.15) = -285.83 \pm 0.04$ kJ/mol were borrowed from [11, 12].

$\Delta_f H^0(298.15)\text{C}_{15}\text{H}_{18}\text{O}_4$ of solid modification was calculated using the formula

$$\begin{aligned} & \Delta_f H^0(298.15)\text{C}_{15}\text{H}_{18}\text{O}_4(\text{s}) \\ & = \Delta_f H^0(298.15)\text{C}_{15}\text{H}_{18}\text{O}_4(1) - \Delta H_{\text{melt}}^0. \end{aligned} \quad (4)$$

The enthalpy of melting ΔH_{melt}^0 was estimated using the Gambill equation [13]

$$\Delta H_{\text{melt}}^0/T_{\text{melt}} = 20.72 \times 10^{0.00324M} \quad (5)$$

and was found to be equal to 62.0 ± 3.0 kJ/mol.

The calculated value of $\Delta_f H^0(298.15)\text{C}_{15}\text{H}_{18}\text{O}_4(\text{s})$ was -200.0 ± 11.0 kJ/mol according to Eq. (4).

CONCLUSIONS

Our results contribute to the physical chemistry of terpenoids and their derivatives, and can be used to study the thermochemical properties of similar biologically active compounds.

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